(1) Conditions of use prescribed, recommended, or suggested by the applicant for the product from the conditions of such use stated in the application;

(2) Articles used as components of the product from those listed in the application;

(3) Composition of the product from that stated in the application;

(4) Methods used in or the facilities and controls used for the manufacture, processing, or packing of the product from such methods, facilities, and controls described in the application;

(5) Labeling from the specimens contained in the application; or

(b) The unexplained omission in whole or in part from an application or from an amendment or supplement to an application or from any record or report required under the provisions of section 512 of the act and § 510.300 or § 510.301 of this chapter of any information obtained from:

(1) Investigations as to the safety, effectiveness, identity, strength, quality, or purity of the drug, made by the applicant on the drug, or

(2) Investigations or experience with the product that is the subject of the application, or any related product, available to the applicant from any source if such information is pertinent to an evaluation of the safety, effectiveness, identity, strength, quality, or purity of the drug, when such omission would bias an evaluation of the safety or effectiveness of the product.

(c) Any nonclinical laboratory study contained in the application was not conducted in compliance with the good laboratory practice regulations as set forth in part 58 of this chapter, and the application fails to include a brief statement of the reason for the noncompliance.

[40 FR 13825, Mar. 27, 1975, as amended at 49 FR 7226, Feb. 28, 1984; 50 FR 7517, Feb. 22, 1985]

EFFECTIVE DATE NOTE: At 67 FR 5057, Feb. 4, 2002, § 514.15 was amended in paragraph (b) by removing ''§ 510.300'' and adding in its place ''§ 514.80'', effective Aug. 5, 2002.

Subpart B—Administrative Actions on Applications

§ 514.80 Records and reports concerning experience with approved new animal drugs.

The following table outlines the purpose for each paragraph of this section:

Purpose	Paragraph and Title
What information must be reported concerning approved NADAs or ANADAs?	514.80(a) Applicability
What authority does FDA have for requesting records and reports? Who is required to establish, maintain, and report required information relating to experiences with a new animal drug? Is information from foreign sources required?	514.80(a)(1)
What records must be established and maintained and what reports filed with FDA?	514.80(a)(2)
What is FDA's purpose for requiring reports?	514.80(a)(3)
Do applicants of Type A medicated articles have to establish, maintain and report information required under § 514.80?	514.80(a)(4)
How do the requirements under § 514.80 relate to current good manufacturing practices?	514.80(a)(5)
	514.80(b) Reporting Requirements
What are the requirements for reporting product/manufacturing defects?	514.80(b)(1) Three-day NADA/ANADA Field Alert Report
	514.80(b)(2) Fifteen-day NADA/ANADA Alert Report
What are the requirements for reporting serious, unexpected and adverse drug experiences?	514.80(b)(2)(i) Initial Report
What are the requirements for followup reporting of serious, unexpected adverse drug experiences?	514.80(b)(2)(ii) Followup Report
What are the requirements for reporting increases in the frequency of serious, expected and unexpected, and adverse drug experiences?	514.80(b)(2)(iii) Summary Report of Increased Frequency of Adverse Drug Experience
What are the requirements for nonapplicants for reporting adverse drug experiences?	514.80(b)(3) Nonapplicant Report

Purpose	Paragraph and Title
What are the general requirements for submission of periodic drug experience reports, e.g., forms to be submitted, submission date and frequency, when is it to be submitted, how many copies? How do I petition to change the date of submission or frequency of submissions?	514.80(b)(4) Periodic Drug Experience Reports
What must be submitted in the periodic drug experience reports?	514.80(b)(4)(i) through (b)(4)(iv)
What distribution data must be submitted? How should the distribution data be submitted?	514.80(b)(4)(i) Distribution Data
What labeling materials should be submitted? How do I report changes to the labeling materials since the last report?	514.80(b)(4)(ii) Labeling
	514.80(b)(4)(iii) Nonclinical Laboratory Studies and Clinical Data Not Previously Reported
What are the requirements for submission of nonclinical laboratory studies?	514.80(b)(4)(iii)(A)
What are the requirements for submission of clinical laboratory data?	514.80(b)(4)(iii)(B)
When must results of clinical trials conducted by or for the applicant be reported?	514.80(b)(4)(iii)(C)
	514.80(b)(4)(iv) Adverse Drug Experiences
How do I report product/manufacturing defects and adverse drug experiences not previously reported to FDA?	514.80(b)(4)(iv)(A)
What are the requirements for submitting adverse drug experiences cited in literature?	514.80(b)(4)(iv)(B)
What are the requirements for submitting adverse drug experiences in postapproval studies and clinical trials?	514.80(b)(4)(iv)(C)
	514.80(b)(5) Other Reporting
Can FDA request that an applicant submit information at different times than stated specifically in this regulation?	514.80(b)(5)(i) Special Drug Experience Report
What are the requirements for submission of advertisement and promotional labeling to FDA?	514.80(b)(5)(ii) Advertisements and Promotional Material
What are the requirements for adding a new distributor to the approved application?	514.80(b)(5)(iii) Distributor's Statement
What labels and how many labels need to be submitted for review?	514.80(b)(5)(iii)(A)
What changes are required and allowed to distributor labeling?	514.80(b)(5)(iii)(A)(I)
What are the requirements for making other changes to the distributor labeling?	514.80(b)(5)(iii)(A)(II)
What information should be included in each new distributor's signed statement?	514.80(b)(5)(iii)(B)(I) through (B)(V)
What are the conditions for submitting information that is common to more than one application? (i.e., can I submit common information to one application?)	514.80(c) Multiple Applications
What information has to be submitted to the common application and related application?	514.80(c)(1) through (c)(4)
What forms do I need? What are Forms FDA 1932 and 2301? How can I get them? Can I use computer-generated equivalents?	514.80(d) Reporting Forms
How long must I maintain Form FDA 1932 and records and reports of other required information, i.e., how long do I need to maintain this information?	514.80(e) Records to be Maintained
What are the requirements for allowing access to these records and reports, and copying by authorized FDA officer or employee?	514.80(f) Access to Records and Reports
How do I obtain Forms FDA 1932 and 2301? Where do I mail FDA's required forms, records, and reports?	514.80(g) Mailing Address
What happens if the applicant fails to establish, maintain, or make the required reports? What happens if the applicant refuses to allow FDA access to, and/or copying and/or verify records and reports?	514.80(h) Withdrawal of Approval
Does an adverse drug experience reflect a conclusion that the report or information constitutes an admission that the drug caused an adverse effect?	514.80(i) Disclaimer

(a) *Applicability.* (1) Each applicant and nonapplicant must establish and maintain indexed, separate, and complete files containing full records of all

information pertinent to safety or effectiveness of a new animal drug that has not been previously submitted as part of the NADA or ANADA. Such records must include information from domestic, as well as foreign sources.

(2) Each applicant must submit reports of data, studies, and other information concerning experience with new animal drugs to the Food and Drug Administration (FDA) for each approved NADA and ANADA, as required in this section. A nonapplicant must submit data, studies, and other information concerning experience with new animal drugs to the appropriate applicant, as required in this section. The applicant, in turn, must report the nonapplicant's data, studies, and other information to FDA. Applicants and nonapplicants must submit data, studies, and other information described in this section from domestic, as well as foreign sources.

(3) FDA reviews the records and reports required in this section to facilitate a determination under section 512(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b) as to whether there may be grounds for suspending or withdrawing approval of the NADA or ANADA.

(4) The requirements of this section also apply to any approved Type A medicated article. In addition, the requirements contained in § 514.80(b)(1), (b)(2), and (b)(4)(iv) apply to any approved Type A medicated article incorporated in animal feeds.

(5) The records and reports referred to in this section are in addition to those required by the current good manufacturing practice regulations in parts 211, 225, and 226 of this chapter.

(b) *Reporting requirements*—(1) *Three-day NADA/ANADA field alert report.* This report provides information pertaining to product and manufacturing defects that may result in serious adverse drug events. The applicant (or nonapplicant through the applicant) must submit the report to the appropriate FDA District Office or local FDA resident post within 3 working days of first becoming aware that a defect may exist. The information initially may be provided by telephone or other telecommunication means, with prompt written followup using Form FDA 1932 ''Veterinary Adverse Drug Reaction, Lack of Effectiveness, Product Defect Report.'' The mailing cover for these reports must be plainly marked ''*3-Day NADA/ANADA Field Alert Report*.''

(2) *Fifteen-day NADA/ANADA alert report*—(i) *Initial report.* This report provides information on each serious, unexpected adverse drug event, regardless of the source of the information. The applicant (or nonapplicant through the applicant) must submit the report to FDA within 15 working days of first receiving the information. The report must be submitted on Form FDA 1932, and its mailing cover must be plainly marked ''*15-Day NADA/ANADA Alert Report*.''

(ii) *Followup report.* The applicant must promptly investigate all adverse drug events that are the subject of 15-day NADA/ANADA alert reports. If this investigation reveals significant new information, a followup report must be submitted within 15 working days of receiving such information. A followup report must be submitted on Form FDA 1932, and its mailing cover must be plainly marked ''*15-Day NADA/ANADA Alert Report Followup*.'' The followup report must state the date of the initial report and provide the additional information. If additional information is sought but not obtained within 3 months of the initial report, a followup report is required describing the steps taken and why additional information was not obtained.

(iii) *Summary report of increased frequency of adverse drug experience.* The applicant must periodically review the incidence of reports of adverse drug experiences to determine if there has been an increased frequency of serious (expected and unexpected) adverse drug events. The applicant must report as soon as possible, but in any case within 15 working days of determining that there is an increased frequency of serious (expected and unexpected) adverse drug events. Summaries of reports of increased frequency of adverse drug events must be submitted in narrative form. The summaries must state the time period on which the increased frequency is based, time period comparisons in determining increased frequency, references to any previously

submitted Form FDA 1932, the method of analysis, and the interpretation of the results. The summaries must be submitted under separate cover and may not be included, except for reference purposes, in a periodic drug experience report. The applicant must evaluate the increased frequency of serious (expected or unexpected) adverse drug events at least as often as reporting of periodic drug experience reports.

(3) *Nonapplicant report.* Nonapplicants must forward reports of adverse drug experiences to the applicant within 3 working days of first receiving the information. The applicant must then submit the report(s) to FDA as required in this section. The nonapplicant must maintain records of all nonapplicant reports, including the date the nonapplicant received the information concerning adverse drug experiences, the name and address of the applicant, and a copy of the adverse drug experience report including the date such report was submitted to the applicant. If the nonapplicant elects to also report directly to FDA, the nonapplicant should submit the report on Form FDA 1932 within 15 working days of first receiving the information.

(4) *Periodic drug experience report.* This report must be accompanied by a completed Form FDA 2301 ''Transmittal of Periodic Reports and Promotional Materials for New Animal Drugs.'' It must be submitted every 6 months for the first 2 years following approval of an NADA or ANADA and yearly thereafter. Reports required by this section must contain data and information for the full reporting period. The 6-month periodic drug experience reports must be submitted within 30 days following the end of the 6-month reporting period. The yearly periodic drug experience reports must be submitted within 60 days of the anniversary date of the approval of the NADA or ANADA. Any previously submitted information contained in the report must be identified as such. For yearly (annual) periodic drug experience reports, the applicant may petition FDA to change the date of submission or frequency of reporting, and after approval of such petition, file such reports on the new filing date or at the new reporting frequency. Also, FDA may require a report at different times or more frequently. The periodic drug experience report must contain the following:

(i) *Distribution data.* Information about the distribution of each new animal drug product, including information on any distributor-labeled product. This information must include the total number of distributed units of each size, strength, or potency (e.g., 100,000 bottles of 100 5-milligram tablets; 50,000 10-milliliter vials of 5 percent solution). This information must be presented in two categories: quantities distributed domestically and quantities exported.

(ii) *Labeling.* Applicant and distributor current package labeling, including package inserts (if any). For large-size package labeling or large shipping cartons, a representative copy must be submitted (e.g., a photocopy of pertinent areas of large feed bags). A summary of any changes in labeling made since the last report (listed by date of implementation) must be included with the labeling or if there have been no changes, a statement of such fact must be included with the labeling.

(iii) *Nonclinical laboratory studies and clinical data not previously reported.*

(A) Copies of in vitro studies (e.g., mutagenicity) and other nonclinical laboratory studies conducted by or otherwise obtained by the applicant.

(B) Copies of published clinical trials of the new animal drug (or abstracts of them) including clinical trials on safety and effectiveness, clinical trials on new uses, and reports of clinical experience pertinent to safety conducted by or otherwise obtained by the applicant. Review articles, papers, and abstracts in which the drug is used as a research tool, promotional articles, press clippings, and papers that do not contain tabulations or summaries of original data are not required to be reported.

(C) Descriptions of, or if available, prepublication manuscripts relating to completed clinical trials conducted by or otherwise known to the applicant. Supporting information is not to be reported. A study must be submitted no later than 1 year after completion of research.

(iv) *Adverse drug experiences.* (A) Product/manufacturing defects and adverse drug experiences not previously reported under § 514.80(b)(1) and (b)(2) must be reported individually on Form FDA 1932.

(B) Reports of adverse drug experiences in the literature must be noted in the periodic drug experience report. A bibliography of pertinent references must be included with the report. Upon FDA's request, the applicant must provide a full text copy of these publications.

(C) Reports of previously not reported adverse drug experiences that occur in postapproval studies must be reported separately from other experiences in the periodic drug experience report and clearly marked or highlighted.

(5) *Other reporting*—(i) *Special drug experience report.* Upon written request, FDA may require that the applicant submit a report required under § 514.80 at different times or more frequently than the timeframes stated in § 514.80.

(ii) *Advertisements and promotional labeling.* The applicant must submit at the time of initial dissemination one set of specimens of mailing pieces and other labeling for prescription and over-the-counter new animal drugs. For prescription new animal drugs, the applicant must also submit one set of specimens of any advertisement at the time of initial publication or broadcast. Mailing pieces and labeling designed to contain product samples must be complete except that product samples may be omitted. Each submission of promotional material must be accompanied by a completed Form FDA 2301.

(iii) *Distributor's statement.* At the time of initial distribution of a new animal drug product by a distributor, the applicant must submit a special drug experience report accompanied by a completed Form FDA 2301 containing the following:

(A) The distributor's current product labeling.

(1) The distributor's labeling must be identical to that in the approved NADA/ANADA except for a different and suitable proprietary name (if used) and the name and address of the distributor. The name and address of the distributor must be preceded by an appropriate qualifying phrase such as ''manufactured for'' or ''distributed by.''

(2) Other labeling changes must be the subject of a supplemental NADA or ANADA as described under § 514.8.

(B) A signed statement by the distributor stating:

(1) The category of the distributor's operations (e.g., wholesale or retail),

(2) That the distributor will distribute the new animal drug only under the approved labeling,

(3) That the distributor will advertise the product only for use under the conditions stated in the approved labeling,

(4) That the distributor will adhere to the records and reports requirements of this section, and

(5) That the distributor is regularly and lawfully engaged in the distribution or dispensing of prescription products if the product is a prescription new animal drug.

(c) *Multiple applications.* Whenever an applicant is required to submit a periodic drug experience report under the provisions of § 514.80(b)(4) with respect to more than one approved NADA or ANADA for preparations containing the same new animal drug so that the same information is required to be reported for more than one application, the applicant may elect to submit as a part of the report for one such application (the primary application) all the information common to such applications in lieu of reporting separately and repetitively on each. If the applicant elects to do this, the applicant must do the following:

(1) State when a report applies to multiple applications and identify all related applications for which the report is submitted by NADA or ANADA number.

(2) Ensure that the primary application contains a list of the NADA or ANADA numbers of all related applications.

(3) Submit a completed Form FDA 2301 to the primary application and each related application with reference to the primary application by NADA/ANADA number and submission date for the complete report of the common information.

(4) All other information specific to a particular NADA/ANADA must be included in the report for that particular NADA/ANADA.

(d) *Reporting forms.* Applicant must report adverse drug experiences and product/manufacturing defects on Form FDA 1932, ''Veterinary Adverse Drug Reaction, Lack of Effectiveness, Product Defect Report.'' Periodic drug experience reports and special drug experience reports must be accompanied by a completed Form FDA 2301 ''Transmittal of Periodic Reports and Promotional Material for New Animal Drugs,'' in accordance with directions provided on the forms. Computer-generated equivalents of Form FDA 1932 or Form FDA 2301, approved by FDA prior to use, may be used. Form FDA 1932 and Form FDA 2301 may be obtained on the Internet at http://www.cvm.fda.gov/cvm, by telephoning the Division of Surveillance (HFV–210), or by submitting a written request to the following address: Food and Drug Administration, Center for Veterinary Medicine, Division of Surveillance (HFV–210), 7500 Standish Pl., Rockville, MD 20855–2764.

(e) *Records to be maintained.* The applicants and nonapplicants must maintain records and reports of all information required by this section for a period of 5 years after the date of submission.

(f) *Access to records and reports.* The applicant and nonapplicant must, upon request from any authorized FDA officer or employee, at all reasonable times, permit such officer or employee to have access to copy and to verify all such required records and reports.

(g) *Mailing addresses.* Completed 15-day alert reports, periodic drug experience reports, and special drug experience reports must be submitted to the following address: Food and Drug Administration, Center for Veterinary Medicine, Document Control Unit (HFV–199), 7500 Standish Pl., Rockville, MD 20855–2764. Three-day alert reports must be submitted to the appropriate FDA district office or local FDA resident post. Addresses for district offices and resident posts may be obtained from the Internet at http://www.fda.gov.

(h) *Withdrawal of approval.* If FDA finds that the applicant has failed to establish the required records, or has failed to maintain those records, or failed to make the required reports, or has refused access to an authorized FDA officer or employee to copy or to verify such records or reports, FDA may withdraw approval of the application to which such records or reports relate. If FDA determines that withdrawal of the approval is necessary, the agency shall give the applicant notice and opportunity for hearing, as provided in § 514.200, on the question of whether to withdraw approval of the application.

(i) *Disclaimer.* Any report or information submitted under this section and any release of that report or information by FDA will be without prejudice and does not necessarily reflect a conclusion that the report or information constitutes an admission that the drug caused or contributed to an adverse event. A person need not admit, and may deny, that the report or information constitutes an admission that a drug caused or contributed to an adverse event.

EFFECTIVE DATE NOTE: At 67 FR 5057, Feb. 4, 2002, § 514.80 was added, effective Aug. 5, 2002.

§ 514.100 Evaluation and comment on applications.

(a) After the filed application has been evaluated, the applicant will be furnished written comment on any apparent deficiencies in the application.

(b) When the description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such new animal drug appears adequate on its face, but it is not feasible to reach a conclusion as to the safety and effectiveness of the new animal drug solely from consideration of this description, the applicant may be notified that an establishment inspection is required to verify their adequacy.

(c) A request for samples of a new animal drug or any edible tissues and byproducts of animals treated with such a drug, shall specify the quantity deemed adequate to permit tests of analytical methods to determine their adequacy for regulatory purposes. The request should be made as early in the 180-day period as possible to assure